BARBARA ANN KARMANOS CANCER INSTITUTE
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THE INFLUENCE OF METABOLIC SYNDROME ON PROSTATE CANCER PROGRESSION AND RISK OF RECURRENCE IN AFRICAN-AMERICAN AND EUROPEAN AMERICAN MEN

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ABSTRACT

Background and Objective: Deaths from prostate cancer (PCa) are more than two times higher among African Americans (AA) than among European Americans (EA). It is likely that both genetic and environmental factors contribute significantly to the racial disparity in PCa progression and mortality. Recent reports suggest a link between PCa and metabolic syndrome, defined as a cluster of features including abdominal obesity, hypertriglyceridemia, low HDL cholesterol, hypertension, and diabetes mellitus. It has been reported that the presence of any three of the above mentioned features are associated with an increase in PCa risk. Certain racial and ethnic groups are predisposed to developing specific features of metabolic syndrome. While AA men are disproportionately afflicted with diabetes and hypertension, EA men are more likely to present with lipid abnormalities. This study aims to evaluate the role of metabolic syndrome in the progression of PCa among AA and EA men as it may contribute significantly to the racial disparity in outcomes post-diagnosis.

Methods: Eligible participants are PCa cases diagnosed on or after January 1, 2004, aged 75 years and younger at diagnosis. All cases have been diagnosed and/or treated at the Karmanos Cancer Institute (KCI) and its associated clinics. All eligible cases complete a questionnaire at the time of their consent to participate in the study and have their height, weight, and waist circumference measured. Medical records are reviewed for validation of self-reported metabolic syndrome features as well as documentation of data related to their PCa diagnosis and treatment. Follow-up of PCa cases occurs every 6 months post-treatment through documentation of biochemical recurrence or the end of the study.

Results: The recruitment for this investigation is ongoing and has been largely successful. Over the past 16 months, we have enrolled a total of 317 men with a participation rate of 85%. Approximately 55% of patients enrolled are AA, with a median age of diagnosis of 61 years. Approximately 33% of AA patients have been classified as having metabolic syndrome (any three of five features) and 26% of EA patients have been classified similarly.

Impact: If metabolic syndrome is an important prognostic indicator in this investigation, then prevention or control of its features may present a sound strategy for the prevention of adverse events among prostate cancer patients. The results of this study may enhance our understanding as to the causes of the racial disparity in outcomes post-prostate cancer diagnosis.

INTRODUCTION

In 1988, Metabolic Syndrome was first described by Reaven as a cluster of conditions that served as risk factors for cardiovascular disease.(1) Several working definitions of metabolic syndrome have developed which include the following features: 1) abdominal obesity, 2) hypertriglyceridemia, 3) low high-density lipoprotein (HDL) cholesterol, 4) high blood pressure and 5) high fasting glucose.

Its been estimated that metabolic syndrome is present in approximately 25% to 35% of adults in the United States over the age of 18 years. Certain racial and ethnic groups are predisposed to developing specific features of metabolic syndrome. Caucasians present most frequently with lipid abnormalities (hypertriglyceridemia and low HDL cholesterol), AA and Asians present with hypertension whereas diabetes is diagnosed most often among Hispanics, Pacific Islanders (PI) and Native Americans (NA).(2) The prevalence of obesity in the United States has increased dramatically over the past four decades, irrespective of race and ethnicity, with approximately one-third of adults characterized as obese (BMI ≥ 30 kg/m^2).(3)

Several reports have suggested a link between metabolic syndrome and prostate cancer and complement a number of studies indicating associations between prostate cancer and body size, insulin levels and insulin resistance.(4) However relatively few studies include adequate numbers of AA men to properly assess whether or not metabolic syndrome is an important risk factor in this group of men already at high risk for developing the disease.(5) Furthermore, no study to date has systematically addressed the issue of metabolic syndrome in predicting risk of recurrence in any racial group.

The specific aims of the investigation include:

I: To examine the association between specific features of metabolic syndrome and the development of aggressive versus non-aggressive prostate cancer in AA and EA men.

II: To examine the association between specific features of metabolic syndrome and prostate cancer recurrence among AA and EA men.

NATIONAL CANCER INSTITUTE

The Meyer L. Prentis Comprehensive Cancer Center of Metropolitan Detroit, operated by the Karmanos Cancer Institute, is a nationally-designated comprehensive cancer center.

METHODS

- Eligible participants are prostate cancer cases diagnosed on or after January 1st, 2004, aged 75 years and younger at date of diagnosis.

- All cases are living, diagnosed and/or treated at KCI, Detroit Medical Center (DMC) and its associated clinics with no history of invasive cancer prior to their diagnosis of prostate cancer and self identified as AA or EA.

- All participants complete a written, self-administered, comprehensive questionnaire at the time of their consent
- Behavioral factors and medical history are assessed up to one year prior to diagnosis gathering age at onset and treatment for any reported medical conditions.
- Each participant has their height, weight, waist and hip circumference measured according to standardized protocol.
- Blood samples are drawn at the time of their next scheduled follow-up appointment coordinating with the physician.
- Serum and DNA extracted from these samples are banked for use in studies investigating the role of genes and biomarkers related to metabolic syndrome and biologic pathways focused on inflammation and insulin resistance.
- Patients are followed for evidence of prostate cancer recurrence through June, 2012.

- The association between specific metabolic syndrome features and risk of aggressive (compared to non-aggressive prostate cancer) will be evaluated using a logistic regression modeling approach.
- Risk of recurrence associated with metabolic syndrome features will be evaluated using Cox proportional hazards regression analyses.

PRELIMINARY RESULTS

Table 1. Prevalence of metabolic syndrome features among study pa

Metabolic Syndrome Feature N(%)	All Patients N=317	African American N=198	Caucasian N=119	p-value†
Hypertension				0.0008
No	91 (29.0)	44 (22.3)	47 (40.2)	
Yes	223 (71.0)	153 (77.7)	70 (59.8)	
Treatment for Hypertension*				0.006
No	23 (10.5)	10 (6.6)	13 (18.8)	
Yes	197 (89.6)	141 (93.4)	56 (81.2)	
Diabetes				0.10
No	236 (75.4)	141 (72.5)	95(80.5)	
Yes	77 (24.6)	54 (27.5)	23 (19.5)	
Treatment for Diabetes*				0.096
No	17 (22.7)	9 (17.3)	8 (34.8)	
Yes	58 (67.3)	43 (82.7)	15 (65.2)	
Hypercholesterolemia				0.079
No	130 (42.2)	88 (46.1)	42 (35.9)	
Yes	178 (57.8)	103 (53.9)	75 (64.1)	
Treatment for hypercholesterolemia				0.67
No	37 (23.0)	20 (21.7)	17 (24.6)	
Yes	124 (77.0)	72 (78.3)	52 (75.4)	
Obesity (BMI ≥30 kg/m^2)‡				0.77
No	192 (61.7)	121 (62.4)	71 (60.7)	
Yes	119 (38.3)	73 (37.6)	46 (39.3)	
Metabolic Syndrome (3+ features)				0.17
No	210 (69.3)	125 (66.5)	85 (73.9)	
Yes	93 (30.7)	63 (33.5)	30 (26.1)	

† Chi-square test of proportional difference between African American and Caucasian patients.
* Among those patients who report a positive history.
‡ Using weight and height gathered from medical records closest to time of diagnosis.
** Excludes missing data.

Table 2. Clinical characteristics and primary treatment

Characteristic	All Patients N=317	African American N=198	Caucasian N=119
Age at diagnosis in years (median and range)	61 (40 – 75)	61 (40 – 75)	62 (47 – 74)
Pre-diagnostic PSA in ng/ml (median and range)	5.9 (0.9 – 6250)	6.15 (0.90 – 6250)	5.19 (1.0 – 1163)
Primary Treatment N (%)			
Radical Prostatectomy	170 (68.0)	110 (67.9)	60 (68.2)
Radiation Therapy	49 (19.6)	32 (19.8)	17 (19.3)
ADT Monotherapy	17 (6.8)	10 (6.2)	7 (8.0)
Other	14 (5.6)	10 (6.2)	4 (4.5)
Biopsy Gleason Grade N (%)			
≤ 6	93 (37.5)	66 (42.0)	27 (29.7)
7 (3+4)	61 (24.6)	39 (24.8)	22 (24.2)
7 (4+3)	38 (15.3)	21 (13.4)	17 (18.7)
≥ 8	56 (22.6)	31 (19.8)	25 (27.5)
Pathologic Gleason Grade N (%)			
≤ 6	55 (21.0)	34 (20.1)	21 (22.6)
7 (3+4)	58 (22.1)	43 (25.4)	15 (16.1)
7 (4+3)	20 (7.6)	14 (8.3)	6 (6.5)
≥ 8	31 (11.8)	16 (9.5)	15 (16.1)
Pathologic T Stage N (%)			
T1c	1 (0.5)	1 (0.5)	0 (0.0)
T2a	6 (2.7)	4 (2.9)	2 (2.4)
T2b	2 (0.9)	0 (0.0)	2 (2.4)
T2c	52 (23.2)	36 (25.9)	16 (18.8)
T3a	21 (9.4)	12 (8.6)	9 (10.7)
T3b	18 (8.0)	9 (6.5)	9 (10.7)
Lymph Node Involvement N (%)			
N1	10 (6.0)	5 (4.9)	5 (7.8)
Metastases N (%)			
M1	37 (22.2)	18 (18.6)	19 (27.1)

- Recruitment, medical record review, and patient follow-up for this investigation is ongoing. At the end of study we anticipate recruitment of 500 patients.
- If metabolic syndrome is an important prognostic indicator, then prevention or control of its features may present a sound strategy for the prevention of adverse events among prostate cancer patients.
- The results of this study may enhance our understanding as to the causes of the racial disparity in outcomes post-diagnosis.

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